ESTIMATING THE INFLUENCE OF MAGNETIZATION TRANSFER EFFECTS ON CEREBRAL BLOOD FLOW QUANTIFICATION IN PSEUDO-CONTINUOUS ARTERIAL SPIN LABELING

Jan Petr[1], Georg Schramm[1], Frank Hofheinz[1], Jens Maus[1], and Jörg van den Hoff[1]
[1]*PET center, Institute of Radiopharmaceutical Cancer Research, Helmholtz-Zentrum Dresden Rossendorf, Dresden, Germany*

TARGET AUDIENCE: Researchers working on arterial spin labeling (ASL) quantification, clinicians using pseudo-continuous ASL (pCASL).
PURPOSE: The magnetization transfer (MT) effects are a known problem in ASL. The labeling pulses have to be designed in such a way to make the MT effects in the static tissue equal during the control and the labeling phase so they cancel out in the difference image. However even if they cancel out perfectly, the MT effects decrease the relaxation time of both tissue and blood. This, therefore, affects relaxation of the perfusion-weighted signal and the measured cerebral blood flow (CBF). It was shown that the MT effects of Q2TIPS bolus saturation pulses can cause important underestimation of CBF[1] and, recently, a model to correct for this was presented[2]. The pCASL sequence is in theory also prone to a similar effect. In this abstract, the MT exchange rate in tissue is measured during the pCASL labeling. The effect on quantified CBF caused by MT is then calculated.
METHODS: **Data:** A healthy volunteer was scanned with a 3T Philips Achieva MR scanner using an 8-channel head-coil. The acquisition protocol consisted of several pCASL[3] and a 3D TFE T1-weighted sequences. Common parameters of the pCASL sequences were TR/TE = 3765/11 ms, FOV = 220×220 mm^2, pixel size = 2.75×2.75 mm^2, 17 slices (6 mm/0.6 mm gap), flip angle 90°, 2 averages (sufficient for investigating MT effects in static tissue), image plane saturation with a 90° pulse before the start of labeling, and no background suppression. Labeling[3] was performed using a Hanning RF-pulse with duration 0.5 ms, tip angle 18°, and interpulse pause 0.5 ms. First, five individual volumes were obtained without labeling and a delay 100, 200, 500, 1000, and 2000 ms between saturation and imaging. Then ten volumes were obtained with labeling durations 100, 200, 500, 1000, and 2000 ms, no additional delay, and labeling gap 10 and 35 mm. Parameters of the 3D TFE sequence were: TR/TE = 1880/3.7 ms, FOV = 192×224 mm^2, 192 sagittal slices, voxel size = 1×1×1 mm^3, and flip angle = 8°. **Preprocessing:** All ASL volumes and the T_1-weighted volume were aligned to the first ASL volume using a 3D rigid registration. The T_1-weighted volume was segmented to gray and white matter (WM) using the SPM8 toolbox. The WM mask was downscaled to get partial volume (PV) fractions for the ASL volumes. **MT estimation:** The three dataset (no labeling, label gap 10 mm and 35 mm) acquired at multiple times were examined separately. The tissue relaxation time T_1 and the equilibrium magnetization M_0 were obtained in each voxel from the control images $M(t)$ for t = 100, 200, 500, 1000, and 2000 ms: $M(t) = M_0(1\text{-}A.exp(-t/T_1))$, where A was the saturation efficiency. The MT forward exchange rate k_A for each pixel was obtained from T_1 and M_0 of the sequence without labeling (no MT effects) and the M_o^{MT} of the sequence with labeling[2] (separately for each label gap): $k_A = (M_0/M_0^{MT}\text{-}1)/T_1$. Mean WM value of k_A was calculated slice-wise using a mask of WM PV fraction exceeding 80 %. The exchange rate of blood $k_{A,b}$ was obtained from the mean WM k_A as it was experimentally measured to be 3.262 times lower in blood than in WM[4]. **CBF simulation:** The rate $k_{A,b}$ was used to calculate the relaxation time of blood during the labeling: $T_{1,b,MT} = 1/(1/T_{1,b}+k_{A,b})$. The ratio between CBFs obtained using the standard model (with $T_{1,b}$ = 1680 ms) and the model that takes the MT effects into account (uses $T_{1,b,MT}$ instead) was calculated: $CBF_{MT} / CBF_{STD} = exp(delay/T_{1,b,MT})/exp(delay/T_{1,b})$. The MT exchange rate actually varied with the distance from the labeling plane (see Results). The exact relaxation of the label was thus computed numerically by splitting the label to segments with 10 ms steps. Motion and relaxation of each segment was calculated individually assuming blood velocity in arteries[5] 15, 20 and 25 cm/s until the arrival to the imaged slice where the label stayed. Labeling duration 1600 ms and delay 1500 ms were used for the simulation.

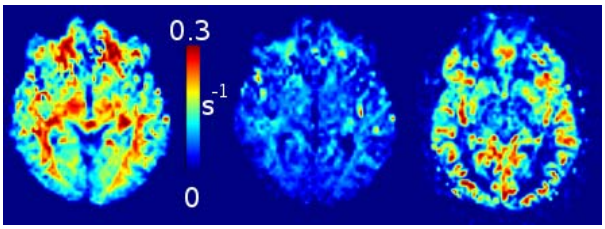

Figure 1. 2nd lowest slice. The MT exchange rate is shown for label gaps 10 mm (left) and 35 mm (middle). A corresponding perfusion-weighted image (right) - 30 averages, labeling time 1600 ms, label delay 1500 ms.

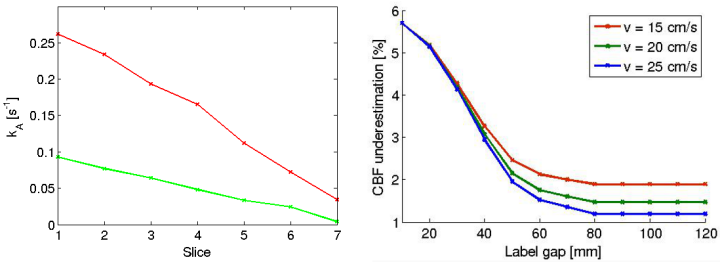

Figure 2. The mean MT exchange rate in white matter (left) is shown for the 7 lowest slices for the label gap 10 mm (red) and 35 mm (green). The calculated CBF underestimation (right) is plotted for different blood velocities and distances of the imaged slice from the labeling plane.

RESULTS: The MT exchange rate for a single slice for both label gaps is shown in Fig 1. The slice-wise mean k_A values in WM are shown in Fig 2 (left). The measured k_A is decreasing with the increasing distance from labeling plane. Note that the distance between slice centers is 6.6 mm and the difference between the two label gaps is 25 mm. That means that the 5th slice of the 10 mm gap sequence is as far from the labeling plane as the 1st slice in the 35 mm gap sequence and so forth. The calculated CBF underestimation is shown in Fig 2 (right). With minimal label gap, the blood velocity has no influence on the CBF underestimation because the label almost immediately enters the imaged slice and stays there. For a label gap wider than 80 mm, the exchange rate in the imaged slice is quite low and thus MT affects mostly the flowing blood. The CBF underestimation is therefore low and does not further increase while widening the label gap.
DISCUSSION: ASL quantification parameters as labeling efficiency are not used as they influence only the absolute value of CBF and not the ratio between CBF_{MT} and CBF_{STD}. MT affects only the closest slices, for the far slices, even the macromolecular-pool protons are off-resonance. It was shown that labeling efficiency of pCASL increases by placing the labeling plane more distal from the imaged volume (up to certain distance)[6]. This can be partly caused also by decreasing the MT effects. Unfortunately, the uneven labeling efficiency for variable label gap prevents to validate our results by comparing CBF obtained with different label gaps and applying the assumed MT effects correction. Apart from validation, the MT effects in pCASL need to be examined in more details in larger population while measuring also the blood-velocity in arteries.
CONCLUSION: MT effects can cause CBF underestimation in pCASL of around 6% especially in the slices close to the labeling plane. Placing the labeling plane farer (60-80 mm) can decreases this effect to around 1-2% only depending on the blood velocity in the arteries.
REFERENCES: **1.** E De Vita et al. MAGMA. 2012; 25(2):113-26. **2.** J Petr et al. Magn Reson Med. 2013; DOI: 10.1002/mrm.25011. **3.** M van Osch et al. Magn Reson Med, 2009; 62(1):165-73. **4.** GJ Stanisz et al. Magn Reson Med 2005;54:507–512. **5.** JC Ferré et al. J Comput Assist Tomogr. 2013;37(2):247-51. **6.** S Aslan et al. Magn Reson Med. 2010; 63(3):765-71.